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* * * * * * * * * *  Welcome to STN International  * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  OCT 23  The Derwent World Patents Index suite of databases on STN
                  has been enhanced and reloaded
 NEWS  4  OCT 30  CHEMLIST enhanced with new search and display field
 NEWS  5  NOV 03  JAPIO enhanced with IPC 8 features and functionality
 NEWS  6  NOV 10  CA/CAplus F-Term thesaurus enhanced
 NEWS  7  NOV 10  STN Express with Discover! free maintenance release Version
                  8.01c now available
 NEWS  8  NOV 20  CA/CAplus to MARPAT accession number crossover limit increased
                  to 50,000
 NEWS  9  DEC 01  CAS REGISTRY updated with new ambiguity codes
 NEWS 10  DEC 11  CAS REGISTRY chemical nomenclature enhanced
 NEWS 11  DEC 14  WPIDS/WPINDEX/WPIX manual codes updated
 NEWS 12  DEC 14  GBFULL and FRFULL enhanced with IPC 8 features and
                  functionality
 NEWS 13  DEC 18  CA/CAplus pre-1967 chemical substance index entries enhanced
                  with preparation role
 NEWS 14  DEC 18  CA/CAplus patent kind codes updated
 NEWS 15  DEC 18  MARPAT to CA/CAplus accession number crossover limit increased
                  to 50,000
 NEWS 16  DEC 18  MEDLINE updated in preparation for 2007 reload
 NEWS 17  DEC 27  CA/CAplus enhanced with more pre-1907 records
 NEWS 18  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS 19  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS 20  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS 21  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS 22  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS 23  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS 24  JAN 29  PHAR reloaded with new search and display fields
 NEWS 25  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 26  FEB 13  CASREACT coverage to be extended
 NEWS 27  Feb 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 28  Feb 15  RUSSIAPAT enhanced with pre-1994 records

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 07:41:44 ON 20 FEB 2007

=> file medline
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

FILE 'MEDLINE' ENTERED AT 07:41:52 ON 20 FEB 2007

 FILE LAST UPDATED: 17 Feb 2007 (20070217/UP).  FILE COVERS 1950 TO DATE.

  All regular MEDLINE updates from November 15 to December 16 have been
  added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R))
  and 2007 tree numbers.

  The annual reload will be available in early 2007.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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=> e sarngadharen m g/au
E1          145     SARNGADHARAN M G/AU
E2            1     SARNGADHARAN MANGALASSERIL G/AU
E3            0 --> SARNGADHAREN M G/AU
E4            1     SARNGREN ANDERS/AU
E5            1     SARNHULT T/AU
E6            4     SARNHULT TORE/AU
E7            2     SARNI A V/AU
E8            1     SARNI ANGELA/AU
E9            3     SARNI C F/AU
E10           2     SARNI C R/AU
E11           3     SARNI D/AU
E12           1     SARNI E/AU

=> s e1
L1          145 "SARNGADHARAN M G"/AU

=> s l1 and gp160
         1548 GP160
L2          11 L1 AND GP160

=> s l2 and gp160/ti
          286 GP160/TI
L3            3 L2 AND GP160/TI

=> d l3,cbib,1-3

L3   ANSWER 1 OF 3     MEDLINE on STN
94358112.    PubMed ID: 8077388.   Enzyme immunoassay using native envelope
     glycoprotein (gp160) for detection of human immunodeficiency virus type
     1 antibodies. Nair B C; Ford G; Kalyanaraman V S; Zafari M; Fang C;
     Sarngadharan M G. (Advanced BioScience Laboratories, Inc., Kensington,
     Maryland 20895. ) Journal of clinical microbiology, (1994 Jun) Vol. 32,
     No. 6, pp. 1449-56.  Journal code: 7505564. ISSN: 0095-1137. Pub. country:
     United States. Language: English.

L3   ANSWER 2 OF 3     MEDLINE on STN
90253924.    PubMed ID: 2187500.   Characterization of the secreted, native
     gp120 and gp160 of the human immunodeficiency virus type 1. Kalyanaraman
     V S; Rodriguez V; Veronese F; Rahman R; Lusso P; DeVico A L; Copeland T;
     Oroszlan S; Gallo R C; Sarngadharan M G. (Bionetics Research Inc.,
     Kensington, MD 20895. ) AIDS research and human retroviruses, (1990 Mar)
     Vol. 6, No. 3, pp. 371-80.  Journal code: 8709376. ISSN: 0889-2229. Pub.
     country: United States. Language: English.

L3   ANSWER 3 OF 3     MEDLINE on STN
89062028.    PubMed ID: 3264172.   A unique human immunodeficiency virus
     culture secreting soluble gp160. Kalyanaraman V S; Pal R; Gallo R C;
     Sarngadharan M G. (Department of Cell Biology, Bionetics Research, Inc.
     Rockville, MD 20850. ) AIDS research and human retroviruses, (1988 Oct)
     Vol. 4, No. 5, pp. 319-29.  Journal code: 8709376. ISSN: 0889-2229. Pub.
     country: United States. Language: English.


=> d his

     (FILE 'HOME' ENTERED AT 07:41:44 ON 20 FEB 2007)

     FILE 'MEDLINE' ENTERED AT 07:41:52 ON 20 FEB 2007
                E SARNGADHAREN M G/AU
L1          145 S E1
L2           11 S L1 AND GP160
L3            3 S L2 AND GP160/TI

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 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE' AT 08:03:07 ON 20 FEB 2007
FILE 'MEDLINE' ENTERED AT 08:03:07 ON 20 FEB 2007
COST IN U.S. DOLLARS                          SINCE FILE       TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                              14.16       14.37

=> e VanCott T C/au
E1            1     VANCOTT MARY LOU/AU
E2            4     VANCOTT T/AU
E3           48 --> VANCOTT T C/AU
E4            2     VANCOTT THOMAS/AU
E5           11     VANCOTT THOMAS C/AU
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E6            1      VANCOTT TOM/AU
E7            1      VANCOTTHEM B/AU
E8            1      VANCOURT/AU
E9            1      VANCOURT B/AU
E10           2      VANCOURT R/AU
E11           2      VANCOURT R B/AU
E12           3      VANCOURT ROBERT/AU

=> s e3-e5
            48 "VANCOTT T C"/AU
             2 "VANCOTT THOMAS"/AU
            11 "VANCOTT THOMAS C"/AU
L4          61 ("VANCOTT T C"/AU OR "VANCOTT THOMAS"/AU OR "VANCOTT THOMAS
               C"/AU)

=> s l4 and (ogp160? or gp160?)
             0 OGP160?
          1557 GP160?
L5          17 L4 AND (OGP160? OR GP160?)

=> d l5,cbib,ab,1-17

L5   ANSWER 1 OF 17     MEDLINE on STN
2004510288.     PubMed ID: 15479439.   Liposome-stabilized oil-in-water
     emulsions as adjuvants: increased emulsion stability promotes induction of
     cytotoxic T lymphocytes against an HIV envelope antigen. Richards Roberta
     L; Rao Mangala; Vancott Thomas C; Matyas Gary R; Birx Deborah L; Alving
     Carl R. (Department of Membrane Biochemistry, Walter Reed Army Institute
     of Research, Silver Spring, MD 20910-7500, USA..
     Roberta.Owens@na.amedd.army.mil) . Immunology and cell biology, (2004 Oct)
     Vol. 82, No. 5, pp. 531-8. Journal code: 8706300. ISSN: 0818-9641. Pub.
     country: Australia. Language: English.
AB   Protective or therapeutic immunity against HIV infection is currently
     believed to require both antibody and CTL responses against the envelope
     protein.  In the present study, the adjuvant activity of a unique
     oil-in-water emulsion, in which liposomes containing lipid A (LA) and
     encapsulated antigen served as the emulsifying agent, was examined in mice
     using oligomeric gp140 (ogp140) derived from the HIV-1 envelope as the
     antigen.  Emulsions rendered either highly stable or unstable by altering
     the ratio of liposomes to oil were used to examine the effect of stability
     of the emulsion on adjuvant activity.  Stable and unstable emulsions had
     similar potencies for inducing both IgG antibodies to ogp140 and
     antigen-specific T-lymphocyte proliferation.  Stable emulsions, but not
     unstable emulsions, induced antigen-specific CTL responses, possibly
     because of the depot effect of the stable emulsions.  Furthermore, stable
     emulsions induced lower IgG2a/IgG1 ratios than the unstable emulsions.  We
     conclude that stable liposomal oil-in-water emulsions provide an effective
     means of obtaining both antibody and CTL responses against an HIV envelope
     antigen.
     Copyright 2004 Australasian Society for Immunology Inc.

L5   ANSWER 2 OF 17     MEDLINE on STN
2003087985.     PubMed ID: 12584337.   Induction of primary virus-cross-reactive
     human immunodeficiency virus type 1-neutralizing antibodies in small
     animals by using an alphavirus-derived in vivo expression system. Dong
     Ming; Zhang Peng Fei; Grieder Franziska; Lee James; Krishnamurthy
     Govindaraj; VanCott Thomas; Broder Christopher; Polonis Victoria R; Yu
     Xiao-Fang; Shao Yiming; Faix Dennis; Valente Patricia; Quinnan Gerald V
     Jr. (Departments of Preventive Medicine and Biometrics, Uniformed Services
     University of the Health Sciences, Bethesda 20814, USA. ) Journal of
     virology, (2003 Mar) Vol. 77, No. 5, pp. 3119-30. Journal code: 0113724.
     ISSN: 0022-538X. Pub. country: United States. Language: English.
AB   We have studied the induction of neutralizing antibodies by in vivo
     expression of the human immunodeficiency virus type 1 (HIV-1) envelope by
     using a Venezuelan equine encephalitis virus (VEE) replicon system with
     mice and rabbits.  The HIV-1 envelope, clone R2, has broad sensitivity to
     cross-reactive neutralization and was obtained from a donor with broadly
     cross-reactive, primary virus-neutralizing antibodies (donor of reference
     serum, HIV-1-neutralizing serum 2 [HNS2]).  It was expressed as gp160,
     as secreted gp140, and as gp160deltaCT with the cytoplasmic tail
     deleted. gp140 was expressed in vitro at a high level and was
     predominantly uncleaved oligomer. gp160deltaCT was released by cells in
     the form of membrane-bound vesicles. gp160deltaCT induced stronger
     neutralizing responses than the other forms.  Use of a helper plasmid for
     replicon particle packaging, in which the VEE envelope gene comprised a
     wild-type rather than a host range-adapted sequence, also enhanced
     immunogenicity.  Neutralizing activity fractionated with immunoglobulin G.
     This activity was cross-reactive among a panel of five nonhomologous
     primary clade B strains and a Chinese clade C strain and minimally
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reactive against a Chinese clade E (circulating recombinant form 1) strain. The comparative neutralization of these strains by immune mouse sera was similar to the relative neutralizing effects of HNS2, and responses induced in rabbits were similar to those induced in mice. Together, these results demonstrate that neutralizing antibody responses can be induced in mice within 2 to 3 months that are similar in potency and cross-reactivity to those found in the chronically infected, long-term nonprogressive donor of HNS2. These findings support the expectation that induction of highly cross-reactive HIV-1 primary virus-neutralizing activity by vaccination may be realized.

L5 ANSWER 3 OF 17 MEDLINE on STN

2001439455. PubMed ID: 11485619. Selective increases in HIV-specific neutralizing antibody and partial reconstitution of cellular immune responses during prolonged, successful drug therapy of HIV infection. Kim J H; Mascola J R; Ratto-Kim S; **VanCott T C**; Loomis-Price L; Cox J H; Michael N L; Jagodzinski L; Hawkes C; Mayers D; Gilliam B L; Birx D C; Robb M L. (Walter Reed Army Institute of Research, Rockville, Maryland 20850, USA.. jkim@hivresearch.org) . AIDS research and human retroviruses, (2001 Jul 20) Vol. 17, No. 11, pp. 1021-34. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Because the immune response to HIV depends on viral gene expression, we examined the HIV-specific immune responses in persons whose viral load after highly active antiretroviral therapy (HAART) was <400 on at least 3 occasions over a 12-month interval. Eleven patients were identified. While there was little change in mean HIV-binding antibody (Ab) titers in this group, two persons mounted increases in HIV envelope-specific binding antibody. Neutralizing antibody (NAb) titers against a panel of HIV-1 primary isolates (BZ167, US1, and cm^{2}37) increased post-HAART (80% neutralization titer against US1, $p = 0.06$; against cm^{2}37, $p = 0.04$). The two persons with large increases in binding antibody also had increases in primary isolate NAb. Roughly half of HAART recipients had significant increases in neutralizing antibody to the primary isolates US1 and cm^{2}37. Compared with CD4-matched, non-HAART controls, there were significant increases in NAb against the subtype B primary isolate US1 ($p < 0.0009$); no increases were seen against more easily neutralized primary isolate BZ167. There were no differences after HAART in antibody-directed cellular cytotoxicity (ADCC). HAART resulted in a partial restoration of lymphoproliferative responses to recall antigens (tetanus and diphtheria). New responses developed to HIV Gag p24. No patient responded to HIV Env **gp160** or gp120 either before or after HAART. The data underscore the lack of functional reconstitution of HIV-specific, CD4-mediated responses despite durable suppression of viral replication. In the setting of stable anti-HIV Ab levels, the development of increased NAb in certain individuals suggests that control of the virus by HAART may assist in immune control of HIV.

L5 ANSWER 4 OF 17 MEDLINE on STN

2000298918. PubMed ID: 10837175. Lack of association between human immunodeficiency virus type 1 antibody in cervicovaginal lavage fluid and plasma and perinatal transmission, in Thailand. Chuachoowong R; Shaffer N; **VanCott T C**; Chaisilwattana P; Siriwasin W; Waranawat N; Vanprapar N; Young N L; Mastro T D; Lambert J S; Robb M L. (HIV/AIDS Collaboration, Ministry of Public Health, Nonthaburi 11000, Thailand.. rfc3@cdc.gov) . The Journal of infectious diseases, (2000 Jun) Vol. 181, No. 6, pp. 1957-63. Electronic Publication: 2000-05-18. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB To determine the association between human immunodeficiency virus type 1 (HIV)-specific antibody and RNA levels in cervicovaginal lavage (CVL) samples and plasma, zidovudine treatment, and perinatal transmission, HIV subtype E **gp160**-specific IgG and IgA were serially measured in a subset of 74 HIV-infected women in a placebo-controlled trial of zidovudine, beginning at 36 weeks of gestation. HIV IgG was detected in 100% of plasma and 97% of CVL samples; HIV IgA was consistently detected in 62% of plasma and 31% of CVL samples. Antibody titers in CVL samples correlated better with the RNA level in CVL samples than with plasma antibody titers. Zidovudine did not affect antibody titers. Perinatal HIV transmission was not associated with antibody in CVL samples or plasma. HIV-specific antibody is present in the cervicovaginal canal of HIV-infected pregnant women; its correlation with the RNA level in CVL fluid suggests local antibody production. However, there was no evidence that these antibodies protected against perinatal HIV transmission.

L5 ANSWER 5 OF 17 MEDLINE on STN

1999075301. PubMed ID: 9859958. Safety and immunogenicity of HIV recombinant envelope vaccines in HIV-infected infants and children. National Institutes of Health-sponsored Pediatric AIDS Clinical Trials Group (ACTG-218). Lambert J S; McNamara J; Katz S L; Fenton T; Kang M; **VanCott T C**; Livingston R; Hawkins E; Moye J Jr; Borkowsky W; Johnson D;

Yogev R; Duliege A M; Francis D; Gershon A; Wara D; Martin N; Levin M; McSherry G; Smith G. (The Johns Hopkins University, Baltimore, Maryland, USA.. lambert@umbi.umd.edu) . Journal of acquired immune deficiency syndromes and human retrovirology : official publication of the International Retrovirology Association, (1998 Dec 15) Vol. 19, No. 5, pp. 451-61. Journal code: 9501482. ISSN: 1077-9450. Pub. country: United States. Language: English.

AB Study objectives were to evaluate the safety and immunogenicity of three HIV recombinant glycoproteins in HIV-infected infants and children between 1 month and 18 years of age with asymptomatic (P-1) infection. Using Chiron rgp 120 (SF-2) 15 or 50 microg; MicroGeneSys rgp 160 (IIIB) 40 or 320 microg; Genentech rgp120 (MN) 75 or 300 microg; or adjuvant control (Alum or MF-59), children were randomized to a double-blind, placebo-controlled, dose-escalating study of vaccine administered intramuscularly at entry and 1, 2, 3, 4, and 6 months later. No adverse events were attributed to study vaccines. Between 30% and 56% of volunteers exhibited a lymphoproliferative response as defined in terms of stimulation index (SI) to vaccine antigens; 65% of vaccinees but none of placebo recipients exhibited moderate or strong responses after enzyme immunoassay to HIV specific antigens. CD4 cell counts and quantitative HIV culture did not differ significantly among vaccine and control groups, nor were differences found among groups in HIV disease progression. The rgp160 and gp120 subunit vaccines were safe and immunogenic in this population.

L5 ANSWER 6 OF 17 MEDLINE on STN

1999059852. PubMed ID: 9841823. Epidemiologic and biologic characterization of a cohort of human immunodeficiency virus type 1 highly exposed, persistently seronegative female sex workers in northern Thailand. Chiang Mai HEPS Working Group. Beyrer C; Artenstein A W; Rugpao S; Stephens H; **VanCott T C**; Robb M L; Rinkaew M; Birx D L; Khamboonruang C; Zimmerman P A; Nelson K E; Natpratan C. (Division of Retrovirology, Walter Reed Army Institute of Research, Bethesda, MD, USA.. cbeyrer@jhsph.edu) . The Journal of infectious diseases, (1999 Jan) Vol. 179, No. 1, pp. 59-67. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB Characterization of persons highly exposed to human immunodeficiency virus (HIV)-1 who remain uninfected may help define protective immunity. Seventeen HIV-1-seronegative Thai female sex workers (CSWs) with epidemiologic evidence of exposure to HIV-1 were studied for humoral immune responses and phenotypic and genotypic analyses of HLA class I and CCR5 allelic profiles. Infected CSWs and low-risk HIV-1-seronegative Thai women were controls. Highly exposed, persistently seronegative (HEPS) CSWs did not differ from HIV-infected CSWs in HIV risks, condom use, or sexually transmitted diseases. Significant differences were seen in humoral immune responses: **gp160**-specific IgA responses were detected in cervicovaginal lavage fluids in 6 of 13 HEPS CSWs but 0 of 21 seronegative subjects. All women had wild-type CCR5. HEPS CSWs were more likely to have the HLA-B18 phenotype and genotype than were matched controls (corrected P=.018). Epidemiologic exposure to HIV-1 without apparent infection, an unusual distribution of HLA class I alleles, and HIV-1 **gp160**-specific IgA responses suggest a biologic basis for this phenomenon.

L5 ANSWER 7 OF 17 MEDLINE on STN

1998453446. PubMed ID: 9780250. Correlation between humoral responses to human immunodeficiency virus type 1 envelope and disease progression in early-stage infection. Loomis-Price L D; Cox J H; Mascola J R; **VanCott T C**; Michael N L; Fouts T R; Redfield R R; Robb M L; Wahren B; Sheppard H W; Birx D L. (H.M. Jackson Foundation, Walter Reed Army Institute of Research, Rockville, MD, USA.. lloomis-price@hiv.hif.org) . The Journal of infectious diseases, (1998 Nov) Vol. 178, No. 5, pp. 1306-16. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB Human immunodeficiency virus (HIV)-1-infected rapid and slow progressors showed differential humoral responses against HIV envelope peptides and proteins early in infection. Sera from slow progressors reacted more strongly with short envelope peptides modeling **gp160NL4**-3, predominantly in gp41. Reactivity to six peptides (in constant regions C3, C4, and C5 of gp120 and in gp41) correlated with slower progression. In a novel association, reactivity to three peptides (in constant regions C1 and C3 and variable region V3 of gp120) correlated with faster progression. Envelope peptide reactivity correlated with subsequent course of disease progression as strongly as did reactivity to gag p24. Patients heterozygous for 32-bp deletions in the CCR5 coreceptor reacted more frequently to an epitope in gp41. Rapid progressors had greater gp120 native-to-denatured binding ratios than did slow progressors. While antibody-dependent cellular cytotoxicity against gp120 did not strongly differentiate the groups, slow progressors showed a broader neutralization pattern against 5 primary virus isolates.

L5 ANSWER 8 OF 17 MEDLINE on STN

1998129366. PubMed ID: 9469464. HIV-1 neutralizing antibodies in the genital and respiratory tracts of mice intranasally immunized with oligomeric **gp160**. **VanCott T C**; Kaminski R W; Mascola J R; Kalyanaraman V S; Wassef N M; Alving C R; Ulrich J T; Lowell G H; Birx D L. (Henry M. Jackson Foundation, Walter Reed Army Institute of Research, Rockville, MD 20850, USA.. tvancott@hiv.hjf.org) . Journal of immunology (Baltimore, Md. : 1950), (1998 Feb 15) Vol. 160, No. 4, pp. 2000-12. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Because mucosal surfaces are a primary route of HIV-1 infection, we evaluated the mucosal immunogenicity of a candidate HIV-1 vaccine, oligomeric **gp160** (o-**gp160**). In prior studies, parenteral immunization of rabbits with o-**gp160** elicited broad neutralizing serum Ab responses against both T cell line-adapted HIV-1 and some primary HIV-1 isolates. In this study, nasal immunization of mice with o-**gp160**, formulated with liposomes containing monophosphoryl lipid A (MPL), MPL-AF, proteosomes, emulsomes, or proteosomes with emulsomes elicited strong **gp160**-specific IgG and IgA responses in serum as well as vaginal, lung, and intestinal washes and fecal pellets. The genital, respiratory, and intestinal Abs were determined to be locally produced. No mucosal immune responses were measurable when the immunogen was given s.c. Abs from sera and from vaginal and lung washes preferentially recognized native forms of monomeric gp120, suggesting no substantial loss in protein tertiary conformation after vaccine formulation and mucosal administration. Inhibition of HIV-1MN infection of H9 cells was found in sera from mice immunized intranasally with o-**gp160** formulated with liposomes plus MPL, proteosomes, and proteosomes plus emulsomes. Formulations of o-**gp160** with MPL-AF, proteosomes, emulsomes, or proteosomes plus emulsomes elicited HIV-1MN-neutralizing Ab in lung wash, and formulations with proteosomes, emulsomes, or proteosomes plus emulsomes elicited HIV-1MN-neutralizing Ab in vaginal wash. These data demonstrate the feasibility of inducing both systemic and mucosal HIV-1-neutralizing Ab by intranasal immunization with an oligomeric **gp160** protein.

L5 ANSWER 9 OF 17 MEDLINE on STN

97347310. PubMed ID: 9203649. Proteosomes, emulsomes, and cholera toxin B improve nasal immunogenicity of human immunodeficiency virus **gp160** in mice: induction of serum, intestinal, vaginal, and lung IgA and IgG. Lowell G H; Kaminski R W; **VanCott T C**; Slike B; Kersey K; Zawoznik E; Loomis-Price L; Smith G; Redfield R R; Amselem S; Birx D L. (Division of Pathology, Walter Reed Army Institute of Research, Washington, DC, USA.) The Journal of infectious diseases, (1997 Feb) Vol. 175, No. 2, pp. 292-301. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB Intranasal immunization of mice with human immunodeficiency virus (HIV) rgp160 complexed to proteosomes improved anti-**gp160** serum IgA and IgG titers, increased the number of **gp160** peptides recognized, and stimulated anti-**gp160** intestinal IgA compared with immunization with uncomplexed rgp160 in saline. These enhanced responses were especially evident when either a bioadhesive nanoemulsion (emulsomes) or cholera toxin B subunit (CTB) was added to the proteosome-rgp160 vaccine. Furthermore, anti-**gp160** IgG and IgA in vaginal secretions and fecal extracts were induced after intranasal immunization with proteosome-rgp160 delivered either in saline or with emulsomes. Formulation of uncomplexed rgp160 with emulsomes or CTB also enhanced serum and selected mucosal IgA responses. Induction of serum, vaginal, bronchial, intestinal, and fecal IgA and IgG by intranasal proteosome-rgp160 vaccines delivered in saline or with emulsomes or CTB is encouraging for mucosal vaccine development to help control the spread of HIV transmission and AIDS.

L5 ANSWER 10 OF 17 MEDLINE on STN

97347307. PubMed ID: 9203646. Mucosal immune responses in four distinct compartments of women infected with human immunodeficiency virus type 1: a comparison by site and correlation with clinical information. Artenstein A W; **VanCott T C**; Sitz K V; Robb M L; Wagner K F; Veit S C; Rogers A F; Garner R P; Byron J W; Burnett P R; Birx D L. (Division of Retrovirology, Walter Reed Army Institute of Research and Henry M. Jackson Foundation, Rockville, Maryland 20850, USA.) The Journal of infectious diseases, (1997 Feb) Vol. 175, No. 2, pp. 265-71. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB Because mucosal immune responses may be important in protection against human immunodeficiency virus type 1 (HIV-1), HIV-1-specific immune responses at mucosal sites in natural infection were compared. Total antibody concentrations and HIV-1-specific binding antibody responses in four distinct mucosal sites and serum were assessed in 41 HIV-infected and 19 HIV-seronegative women. HIV-1 **gp160**-specific IgG responses were detected in >99% of mucosal samples in infected subjects, with the highest titers in genital secretions. HIV-1-specific IgA was detected in the

majority of endocervical secretions (94%) and nasal washes (95%) but less often in vaginal washes (51%) and parotid saliva (38%). There was no significant correlation between mucosal immune response and most clinical factors. Based on methodologic considerations, frequencies of detection, and HIV-1-specific responses, nasal washes and genital secretions may each provide important measures of HIV-1-specific mucosal immune responses in infected women.

L5 ANSWER 11 OF 17 MEDLINE on STN

97296236. PubMed ID: 9151820. Antibodies with specificity to native gp120 and neutralization activity against primary human immunodeficiency virus type 1 isolates elicited by immunization with oligomeric **gp160**. **VanCott T C**; Mascola J R; Kaminski R W; Kalyanaraman V; Hallberg P L; Burnett P R; Ulrich J T; Rechtman D J; Birx D L. (Henry M. Jackson Foundation, Rockville, Maryland 20850, USA.. tvancott@hiv.hjf.org) . Journal of virology, (1997 Jun) Vol. 71, No. 6, pp. 4319-30. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Current human immunodeficiency virus type 1 (HIV-1) envelope vaccine candidates elicit high antibody binding titers with neutralizing activity against T-cell line-adapted but not primary HIV-1 isolates. Serum antibodies from these human vaccine recipients were also found to be preferentially directed to linear epitopes within gp120 that are poorly exposed on native gp120. Systemic immunization of rabbits with an affinity-purified oligomeric **gp160** protein formulated with either Alhydrogel or monophosphoryl lipid A-containing adjuvants resulted in the induction of high-titered serum antibodies that preferentially bound epitopes exposed on native forms of gp120 and **gp160**, recognized a restricted number of linear epitopes, efficiently bound heterologous strains of monomeric gp120 and cell surface-expressed oligomeric gp120/gp41, and neutralized several strains of T-cell line-adapted HIV-1. Additionally, those immune sera with the highest oligomeric **gp160** antibody binding titers had neutralizing activity against some primary HIV-1 isolates, using phytohemagglutinin-stimulated peripheral blood mononuclear cell targets. Induction of an antibody response preferentially reactive with natively folded gp120/**gp160** was dependent on the tertiary structure of the HIV-1 envelope immunogen as well as its adjuvant formulation, route of administration, and number of immunizations administered. These studies demonstrate the capacity of a soluble HIV-1 envelope glycoprotein vaccine to elicit an antibody response capable of neutralizing primary HIV-1 isolates.

L5 ANSWER 12 OF 17 MEDLINE on STN

97240800. PubMed ID: 9120313. Vaccine-specific antibody responses induced by HIV-1 envelope subunit vaccines. Pincus S H; Messer K G; Cole R; Ireland R; **VanCott T C**; Pinter A; Schwartz D H; Graham B S; Gorse G J. (Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, Hamilton, MT 59840, USA.. spincus@montana.edu) . Journal of immunology (Baltimore, Md. : 1950), (1997 Apr 1) Vol. 158, No. 7, pp. 3511-20. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The first generation of candidate vaccines to prevent HIV infection consisted of recombinant envelope proteins (Env, gp120, and **gp160**) derived from a single laboratory strain of HIV, designated IIIB/LAV, but produced with different expression systems. In this study we examined the fine specificity of the human Ab response to each vaccine and compared them to the responses of laboratory workers infected with the same strain of HIV. The best responders from each vaccine protocol were studied and compared. Detailed comparisons of the fine specificity of the Ab response were possible because all immunologic assays were performed using homologous recombinant proteins, peptides, and virus stocks. Although the total amounts of anti-Env Ab were comparable, the groups exhibited significant differences in epitope specificity, avidity, and functional capacity of the Ab response. The data demonstrate that the form of the immunogen (e.g., live virus or recombinant protein) is important in determining the quality of the Ab response. Conclusions are also drawn regarding characteristics of the anti-HIV-neutralizing Ab response. These studies represent one of the most detailed analyses of the human Ab response to any Ag and have implications for the development of vaccines for HIV as well as for other microbial pathogens.

L5 ANSWER 13 OF 17 MEDLINE on STN

97046189. PubMed ID: 8891111. Human immunodeficiency virus type 1 neutralizing antibody serotyping using serum pools and an infectivity reduction assay. Mascola J R; Louder M K; Surman S R; **Vancott T C**; Yu X F; Bradac J; Porter K R; Nelson K E; Girard M; McNeil J G; McCutchan F E; Birx D L; Burke D S. (Division of Retrovirology, Walter Reed Army Institute of Research, Rockville, Maryland 20850, USA.) AIDS research and human retroviruses, (1996 Sep 20) Vol. 12, No. 14, pp. 1319-28. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language:

English.

AB Classification of human immunodeficiency virus type 1 (HIV-1) by neutralization serotype may be important for the design of active and passive immunization strategies. Neutralizing antibody serotyping is hindered by the lack of standard reagents and assay format, and by the weak activity of many individual sera. To facilitate cross-clade neutralization analysis, we used an infectivity reduction assay (IRA) and selected clade-specific serum (or plasma) pools from subjects infected with clade B and E HIV-1, respectively. Several serum pools were utilized; some were selected for strong neutralizing activity against intraclade viruses and others were derived from conveniently available samples. Against a panel of 51 clade B and E viruses, serum pools displayed strong neutralization of most intraclade viruses and significantly diminished cross-clade neutralization. Results were confirmed against a blinded panel of 20 viruses. The data indicate that the phylogenetic classification of virus subtypes B and E corresponds to two distinct neutralization serotypes. This approach to neutralizing antibody serotyping may be useful in defining the antigenic relationship among viruses from other clades.

L5 ANSWER 14 OF 17 MEDLINE on STN

96435813. PubMed ID: 8838699. V3 seroreactivity and sequence variation: tracking the emergence of V3 genotypic variation in HIV-1-infected patients. Michael N L; Davis K E; Loomis-Price L D; **VanCott T C**; Burke D S; Redfield R R; Birx D L. (Division of Retrovirology, Walter Reed Army Institute of Research, Washington, DC, USA.) AIDS (London, England), (1996 Feb) Vol. 10, No. 2, pp. 121-9. Journal code: 8710219. ISSN: 0269-9370. Pub. country: United States. Language: English.

AB OBJECTIVE: To investigate the relationship between V3-specific immune responses and viral quasispecies evolution in 10 HIV-1-seropositive patients enrolled in a phase I trial of recombinant **gp160**. METHODS: Serologic responses to the HIVLAI V3 loop and autologous V3 loop DNA sequences were sequentially determined over a 3-4-year interval. RESULTS: Six patients either seroconverted or had a > or = 42-fold boost in titer to the V3 reagent associated with an average of 3.2 amino-acid changes in their autologous V3 loops. Four patients with < or = 11-fold change in titer to the V3 loop showed an average of 0.75 amino-acid changes. Attempts to measure autologous V3 loop responses in four patients using a peptide enzyme-linked immunosorbent assay technique did not show a distinct binding preference for autologous versus heterologous V3 loop peptides. Thus, we interpret seroreactivity to the heterologous HIVLAI V3 loop to reflect the broadness of the V3 immune response rather than a direct measure of epitope-specific immune pressure. CONCLUSIONS: These data suggest that the broadness of serologic responses to viral epitopes are reflected in the rate of evolution of their cognate coding sequences and support the view that the immune response to HIV-1 results in the continuous selection of new viral variants during the course of disease.

L5 ANSWER 15 OF 17 MEDLINE on STN

96003456. PubMed ID: 7561123. Lack of induction of antibodies specific for conserved, discontinuous epitopes of HIV-1 envelope glycoprotein by candidate AIDS vaccines. **VanCott T C**; Bethke F R; Burke D S; Redfield R R; Birx D L. (Division of Retrovirology, Walter Reed Army Institute of Research, Rockville, MD, USA.) Journal of immunology (Baltimore, Md. : 1950), (1995 Oct 15) Vol. 155, No. 8, pp. 4100-10. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We examined the humoral immune response in both HIV-1 infected and uninfected volunteers immunized with candidate HIV-1 recombinant envelope subunit vaccines (Genentech gp120IIIB, MicroGeneSys **gp160IIIB**, or ImmunoAG **gp160IIIB**). Immunization of both HIV-1 infected and uninfected volunteers with these immunogens resulted in the induction of Abs preferentially reactive with epitopes accessible on a denatured form of gp120. While sera from HIV-1 uninfected gp120/**gp160IIIB** vaccinees bound gp120/gp41, which was expressed on the surface of H9 cells infected with HIV-1IIIB, minimal binding to HIV-1MN or HIV-1RF infected cells was obtained. Induction of qualitatively similar immune responses by these immunogens would not have been predicted based on their different tertiary structures. These data indicate a restriction of the immune response to linear, conserved epitopes poorly accessible on both monomeric gp120 and cell-surface expressed oligomeric gp120/gp41 and a lack of Abs specific for conformational epitopes conserved across divergent HIV-1 strains. Poor recognition of HIV-1 envelope tertiary and quaternary structure may explain the restricted neutralization profiles of vaccinee sera against laboratory-adapted strains of HIV-1 and their inability to neutralize primary HIV-1 isolates. Alternate immunogens or reformulations with the capacity to elicit Abs that preferentially bind to natively folded gp120 should be investigated and correlated with their ability to neutralize more diverse laboratory-adapted and primary HIV-1 isolates.

L5 ANSWER 16 OF 17 MEDLINE on STN
95325634. PubMed ID: 7602128. Characterization of a soluble, oligomeric HIV-1 **gp160** protein as a potential immunogen. **VanCott T C**; Veit S C; Kalyanaraman V; Earl P; Birx D L. (Division of Retrovirology, Walter Reed Army Institute of Research, Rockville, MD 20850, USA.) Journal of immunological methods, (1995 Jun 14) Vol. 183, No. 1, pp. 103-17. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB We have assessed the oligomeric structure and antigenic properties of an affinity purified **gp160** protein (oligo-**gp160**) using biosensor technology. Sucrose gradient purification analysis identified the existence of tetrameric, dimeric and monomeric forms of the protein. Reactivity to a broad panel of monoclonal antibodies specific for oligomeric **gp160**, discontinuous epitopes within monomeric gp120 and several linear epitopes within gp120 (V3) and gp41 was demonstrated. International sera from several countries, where HIV-1 clades A-F are prevalent, including type O from Cameroon, were reactive with oligo-**gp160** indicating conserved antigenic epitopes. Enhanced immunologic reactivity per **gp160** molecule was obtained with oligo-**gp160** as compared to other current HIV-1(IIIB) subunit monomeric envelope gp120/**gp160** immunogens suggesting higher HIV-1 envelope protein mimicry. HIV-1 antibodies from sera during acute HIV-1 infection were detectable by oligo-**gp160** prior to detection with either a recombinant, monomeric gp120 protein or several commercial HIV-1 screening kits suggesting antibodies sensitive to oligomeric **gp160** structure may be present earlier in infection. The oligomeric nature of this **gp160** protein preparation and high reactivity with divergent mAbs and HIV-1 sera support the use of this protein as an HIV-1 immunogen.

L5 ANSWER 17 OF 17 MEDLINE on STN
92166405. PubMed ID: 1538140. Real-time biospecific interaction analysis of antibody reactivity to peptides from the envelope glycoprotein, **gp160**, of HIV-1. **VanCott T C**; Loomis L D; Redfield R R; Birx D L. (Department of Retroviral Research, Walter Reed Army Institute of Research, Washington, DC 20850.) Journal of immunological methods, (1992 Feb 5) Vol. 146, No. 2, pp. 163-76. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB A new assay designed to quantitate antibody reactivity to specific peptides using biospecific interaction analysis (BIAcore) has been developed. Peptides of various lengths (15-40 amino acids) and isoelectric points (pI = 4.5-13) were covalently linked (immobilized) to a biosensor and interacted with polyclonal human sera. The immobilization procedure was highly reproducible, with bound peptides retaining high antibody reactivity. The assay was rapid, requiring only 25-30 min to immobilize the peptide and 2-8 min for each subsequent peptide/serum binding interaction. The same peptide surface has been used for up to 90 cycles of serum binding and regeneration with only a 0.3% decay in reactivity over cycle number. The quantitative BIAcore signal, measuring peptide/antibody binding interactions, was directly related to the antigen/antibody concentrations within the biosensor. The assay allowed interactants to be studied in their native form and without the need of additional secondary detection antibodies. Correlation between conventional peptide ELISA and BIAcore was obtained. The BIAcore linear range persisted over a series of eight two-fold dilutions. This extended linear dynamic response range is an improvement over conventional ELISA measurements. The sensitivity for monoclonal antibody detection is similar to conventional ELISAs and 4.9 ng/ml was readily detected.

```
=> e sarngadharan m g/au
E1            1     SARNGADHARAN G/AU
E2            3     SARNGADHARAN M/AU
E3          145 --> SARNGADHARAN M G/AU
E4            1     SARNGADHARAN MANGALASSERIL G/AU
E5            1     SARNGREN ANDERS/AU
E6            1     SARNHULT T/AU
E7            4     SARNHULT TORE/AU
E8            2     SARNI A V/AU
E9            1     SARNI ANGELA/AU
E10           3     SARNI C F/AU
E11           2     SARNI C R/AU
E12           3     SARNI D/AU

=> s e2-e4
              3 "SARNGADHARAN M"/AU
            145 "SARNGADHARAN M G"/AU
              1 "SARNGADHARAN MANGALASSERIL G"/AU
L6          149 ("SARNGADHARAN M"/AU OR "SARNGADHARAN M G"/AU OR "SARNGADHARAN
                MANGALASSERIL G"/AU)
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=> s l6 and (HIV or human immunodeficiency virus)
        167851 HIV
       1454701 HUMAN
        126599 IMMUNODEFICIENCY
        426888 VIRUS
         50401 HUMAN IMMUNODEFICIENCY VIRUS
                 (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)
L7          51 L6 AND (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)

=> s l7 and (gp160? or ogp160? or gp140? or env?)
          1557 GP160?
             0 OGP160?
           314 GP140?
        450653 ENV?
L8          20 L7 AND (GP160? OR OGP160? OR GP140? OR ENV?)

=> d l8,cbib,ab,1-20

L8   ANSWER 1 OF 20      MEDLINE on STN
96207417.    PubMed ID: 8615032.   Covalently crosslinked complexes of human
     immunodeficiency virus type 1 (HIV-1) gp120 and CD4 receptor elicit
     a neutralizing immune response that includes antibodies selective for
     primary virus isolates. Devico A; Silver A; Thronton A M; Sarngadharan M
     G; Pal R. (Advanced BioScience Laboratories, Inc., 5510 Nicholson Lane,
     Kensington, Maryland, 20895, USA. ) Virology, (1996 Apr 1) Vol. 218, No.
     1, pp. 258-63.  Journal code: 0110674. ISSN: 0042-6822. Pub. country:
     United States. Language: English.
AB   Specific conformational changes in the envelope glycoprotein gp120 of
     the human immunodeficiency virus type-1 (HIV-1) may be critical
     for eliciting a broadly neutralizing immune response against primary virus
     isolates. Since the interaction of gp120 with its receptor, CD4, induces
     conformational perturbations in both molecules, gp120-CD4 complexes should
     present unique immunogenic features that may include novel epitopes for
     broadly neutralizing antibodies. To test this hypothesis, we raised
     polyclonal antiserum against covalently crosslinked gp120-CD4 complexes in
     a goat and examined the ability of the anti-complex antibodies to
     neutralize primary and laboratory-adapted HIV-1 isolates. In cell-free
     neutralization assays with HIV-1MN, the antiserum demonstrated the
     ability to neutralize primary virus more effectively than the
     laboratory-adapted isolate. The neutralizing capacity of the anti-complex
     serum extended to primary isolates from distant genetic clades A, D, and
     E, although the degree of neutralization was found to vary among the
     clades. The neutralizing activity of the serum was composed of two
     components. The first component included anti-CD4 antibodies that
     recognized epitopes outside the gp120 binding site; the second was
     independent of CD4 reactivity and was retained after removal of cell
     surface anti-CD4 reactivity by repeated absorption with CD4-positive
     cells. These results demonstrate that gp120-CD4 complexes can elicit a
     unique polyclonal antibody response that is relevant to the neutralization
     of primary isolates of HIV-1.

L8   ANSWER 2 OF 20      MEDLINE on STN
95373192.    PubMed ID: 7544051.   Monoclonal antibodies raised against
     covalently crosslinked complexes of human immunodeficiency virus
     type 1 gp120 and CD4 receptor identify a novel complex-dependent epitope
     on gp 120. DeVico A L; Rahman R; Welch J; Crowley R; Lusso P;
     Sarngadharan M G; Pal R. (Advanced BioScience Laboratories, Inc.,
     Kensington, Maryland 20895, USA. ) Virology, (1995 Aug 20) Vol. 211, No.
     2, pp. 583-8.  Journal code: 0110674. ISSN: 0042-6822. Pub. country:
     United States. Language: English.
AB   The binding of the human immunodeficiency virus type 1 (HIV-1)
     envelope glycoprotein, gp120, to its cell surface receptor, CD4,
     represents a molecular interaction involving distinct alterations in
     protein structure. Consequently, the pattern of epitopes presented on the
     gp120-CD4 complex should differ from those on free gp120. To investigate
     this concept, mice were immunized with covalently crosslinked complexes of
     viral HIV-1IIIBgp120 and soluble CD4. Two monoclonal antibodies (MoAbs)
     obtained from the immunized mice exhibited a novel epitope specificity.
     The MoAbs were marginally reactive with HIV-1IIIBgp120, highly reactive
     with gp120-CD4 complexes, and unreactive with soluble CD4. The same
     pattern of reactivity was seen in solid-phase assays using
     HIV-1(451)gp120. A similar specificity for complexes was evident in
     flow cytometry experiments, in which MoAb reactivity was dependent upon
     the attachment of gp120 to CD4-positive cells. In addition, MoAb
     reactivity was detected upon the interaction of CD4 receptors with
     purified HIV-1IIIB virions. Notably, seroantibodies from HIV-positive
     individuals competed for MoAb binding, indicating that the epitope is
     immunogenic in humans. The results demonstrated that crosslinked
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gp120-CD4 complexes elicit antibodies to cryptic gp120 epitopes that are exposed during infection in response to receptor binding. These findings may have important implications for the consideration of **HIV envelope**-receptor complexes as targets for virus neutralization.

L8 ANSWER 3 OF 20 MEDLINE on STN

94358112. PubMed ID: 8077388. Enzyme immunoassay using native **envelope** glycoprotein (**gp160**) for detection of **human immunodeficiency virus** type 1 antibodies. Nair B C; Ford G; Kalyanaraman V S; Zafari M; Fang C; **Sarngadharan M G**. (Advanced BioScience Laboratories, Inc., Kensington, Maryland 20895.) Journal of clinical microbiology, (1994 Jun) Vol. 32, No. 6, pp. 1449-56. Journal code: 7505564. ISSN: 0095-1137. Pub. country: United States. Language: English.

AB An enzyme immunoassay using the purified native **gp160** for the detection of **human immunodeficiency virus** type 1 (**HIV**-1) antibody was developed. This assay was determined to be highly specific, since (i) 157 serum samples that were confirmed negative by Western blot (immunoblot) (WB) were negative, (ii) 41 serum samples from populations with medical conditions that might cause nonspecific assay reactivity were all negative, and (iii) all 15 serum samples that showed false-positive reactions in one or more commercial **HIV**-1 screening tests were negative. The assay gave 100% specificity with a randomly selected and unlinked panel of 1,000 serum samples from healthy blood donors. The sensitivity of the assay was assessed by testing 238 samples confirmed as **HIV**-1 antibody positive by a standardized WB assay. All 238 serum samples (100%) were reactive in the native **gp160** assay. In a dilution panel of 14 weakly WB-positive serum samples, 7 samples reacted two-to fivefold more strongly in the **gp160** assay than in a virus lysate-based assay; the remaining 7 samples gave comparable reactivities in the two tests. The reactivities of 13 of these 14 serum samples in the **gp160** assay were higher than in a commercial enzyme immunoassay that uses a recombinant **envelope** protein as the antigen. The native **gp160** assay was more sensitive to identify seroconversion. In a well-characterized panel of sequential blood samples from a seroconverter, the new assay detected antibodies at least one sample ahead of the other commercial assays tested.

L8 ANSWER 4 OF 20 MEDLINE on STN

94071894. PubMed ID: 8250888. Glycoprotein of **human immunodeficiency virus** type 1 synthesized in chronically infected Molt3 cells acquires heterogeneous oligosaccharide structures. Pal R; di Marzo Veronese F; Nair B C; Rittenhouse S; Hoke G; Mumbauer S; **Sarngadharan M G**. (Advanced BioScience Laboratories, Inc., Kensington, Maryland 20895.) Biochemical and biophysical research communications, (1993 Nov 15) Vol. 196, No. 3, pp. 1335-42. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Diversity of oligosaccharide structures on the glycoprotein of **HIV**-1 was studied in individual clones of Molt3 cells chronically infected with **HIV**-1IIIB. A glycoprotein of molecular weight 140 kD (**gp140**) was found to be shed into the medium from one of these clones, which unlike normally processed gp120, contained significant proportions of endo H resistant oligosaccharides. Treatment of infected cells with the inhibitors of oligosaccharide trimming enzymes affected the glycosylation pattern as well as the secretion of the glycoprotein into the medium. The exposure of the principal neutralizing domain (PND) on the surface of **gp140**, as measured by its accessibility to thrombin cleavage, was comparable to that observed with gp120. Sera obtained from mice inoculated with purified **gp140** contained high titered anti-V3 antibodies and blocked **HIV**-1IIIB-induced syncytium formation. These results demonstrate that although glycosylation of viral glycoproteins is governed by the host cell glycosyl transferases, glycoprotein secreted from biological clones of the same host cells acquires different oligosaccharide structures. Exposure and immunogenicity of the PND in one such glycosylation variant are comparable to the normally processed gp120 molecule.

L8 ANSWER 5 OF 20 MEDLINE on STN

93276574. PubMed ID: 8503188. Conformational perturbation of the **envelope** glycoprotein gp120 of **human immunodeficiency virus** type 1 by soluble CD4 and the lectin succinyl Con A. Pal R; DeVico A; Rittenhouse S; **Sarngadharan M G**. (Advanced BioScience Laboratories, Incorporated, Department of Cell Biology, Kensington, Maryland 20895.) Virology, (1993 Jun) Vol. 194, No. 2, pp. 833-7. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB We have studied perturbation of the gp120/gp41 **envelope** complex of **HIV**-1 in the presence of the mannose-specific lectin succinyl Con A (SC) and compared the effect with that observed in the presence of soluble CD4 (sCD4). SC did not inhibit the binding of gp120 to CD4. Both sCD4 and SC inhibited syncytium formation induced by **HIV**-1-infected

Molt3/**HIV**-1IIIB cells. The infectivity of **HIV**-1 was markedly reduced when the virions were preincubated with SC or when SC was mixed simultaneously with virus and cells. The conformation of gp120 was altered in the presence of SC as evidenced by an increased susceptibility of the principal neutralizing epitope (V3 loop) to thrombin digestion. SC treatment of [35S]-methionine-labeled virions derived from Molt3/**HIV**-1IIIB cells resulted in the dissociation of gp120 from the viral membrane. The effect was less pronounced than that observed with sCD4. These results suggest that although interacting with different regions of gp120, the mannose-specific lectin alters the conformation of the glycoprotein in a manner similar to that induced by sCD4, causing destabilization of the gp120/gp41 complex.

L8 ANSWER 6 OF 20 MEDLINE on STN

93186358. PubMed ID: 1284059. Characterization of a neutralizing monoclonal antibody to the external glycoprotein of **HIV**-1. Pal R; di Marzo Veronese F; Nair B C; Rahman R; Hoke G; Mumbauer S W; **Sarngadharan M G**. (Advanced BioScience Laboratories, Kensington, Md 20895.) Intervirology, (1992) Vol. 34, No. 2, pp. 86-93. Journal code: 0364265. ISSN: 0300-5526. Pub. country: Switzerland. Language: English.

AB The major neutralizing epitope on the external glycoprotein of **HIV**-1 was studied with an **envelope**-specific monoclonal antibody and with a human serum positive for antibodies to **HIV**-1 proteins, both of which were able to neutralize virus infectivity. The monoclonal antibody reacted specifically with gp120 from **HIV**-1IIIB, and was shown to neutralize infection of CEM cells by cell-free virions, and inhibited the formation of syncytia normally observed when uninfected cells are cocultured with **HIV**-1-infected cells. Similar neutralization of viral infection and inhibition of syncytia formation was also demonstrated by the **HIV**-1-antibody-positive human serum. By examining a number of overlapping peptides from a region of **HIV**-1 gp120 known to contain a neutralizing epitope, this epitope was localized between amino acids 307 and 320 (V3 loop) in the external glycoprotein molecule. The monoclonal antibody did not interfere with the binding of gp120 to CD4, or with the subsequent step of CD4-induced shedding of gp120 from the viral **envelope**. However, it blocked the proteolytic cleavage of the V3 loop by thrombin, suggesting that the antibody may be inhibiting the interaction of the loop with other membrane-bound proteins.

L8 ANSWER 7 OF 20 MEDLINE on STN

92368730. PubMed ID: 1380259. Delineation of immunoreactive, conserved regions in the external glycoprotein of the **human immunodeficiency virus** type 1. di Marzo Veronese F; Rahman R; Pal R; Boyer C; Romano J; Kalyanaraman V S; Nair B C; Gallo R C; **Sarngadharan M G**. (Department of Cell Biology, Advanced BioScience Laboratories, Inc., Kensington, MD 20895.) AIDS research and human retroviruses, (1992 Jun) Vol. 8, No. 6, pp. 1125-32. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Immunization of mice and rats with purified external glycoprotein gp120 from two divergent **human immunodeficiency virus** type 1 (**HIV**-1) isolates resulted in the development of seven hybridomas secreting monoclonal antibodies able to recognize regions of gp120 which are common among divergent strains of **HIV**-1. These monoclonal antibodies cross-reacted with **env** glycoproteins from one African (Rutz), one Haitian (RF), and three North American viral isolates, namely IIIB, MN, and 451 by either immunoblot or radioimmunoprecipitation assays. All recognized denatured gp120 in immunoblots with the exception of one which required a conformationally intact glycoprotein for reactivity. The gp120 epitopes identified by these antibodies were mapped by screening of an **env** gene library in the lambda gt11 expression system. Three out of four epitopes were found to reside in the amino-terminal half of gp120 (Cys9 to Cys35, Thr44 to Glu72 and Val108 to Met130), the other was located in the middle region (Thr221 to Ser255). By virtue of their extent of cross-reactivity these reagents might provide a unique resource for the detection of new viral isolates related to **HIV**-1.

L8 ANSWER 8 OF 20 MEDLINE on STN

92030393. PubMed ID: 1718346. Brefeldin A inhibits the processing and secretion of **envelope** glycoproteins of **human immunodeficiency virus** type 1. Pal R; Mumbauer S; Hoke G M; Takatsuki A; **Sarngadharan M G**. (Department of Cell Biology, Advanced BioScience Laboratories, Kensington, MD 20895.) AIDS research and human retroviruses, (1991 Aug) Vol. 7, No. 8, pp. 707-12. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB The processing and secretion of the **envelope** glycoproteins of **human immunodeficiency virus** type 1 (**HIV**-1) were studied in chronically infected T cells and in primary macrophages treated with an antiviral antibiotic brefeldin A (BFA). BFA blocks the egress of proteins from the endoplasmic reticulum and has a profound effect on the structure of

cis/medial Golgi. In MOLT-3 cells infected with the IIIB strain of **HIV**-1 (MOLT-3/IIIB), BFA inhibited the intracellular processing of **gp160**. The secretion of **envelope** proteins from these cells was significantly inhibited in the presence of BFA. The gag proteins, on the other hand, were processed and secreted normally. BFA also inhibited the proteolytic processing of **gp160** in primary macrophages infected with **HIV**-1. The infectivity of virus pelleted from the medium of MOLT-3/IIIB cells treated with BFA was markedly lower than that obtained from untreated cells. These results demonstrate that the proteolytic processing of **gp160** in **HIV**-1-infected cells takes place after the glycoprotein exists the endoplasmic reticulum and that the transport of glycoprotein to the cell surface is required for assembly of complete **HIV**-1 particles.

L8 ANSWER 9 OF 20 MEDLINE on STN

91250502. PubMed ID: 2040664. Lateral diffusion of CD4 on the surface of a human neoplastic T-cell line probed with a fluorescent derivative of the **envelope** glycoprotein (gp120) of **human immunodeficiency virus** type 1 (**HIV**-1). Pal R; Nair B C; Hoke G M; **Sarngadharan M G**; Edidin M. (Department of Cell Biology, Advanced BioScience Laboratories, Inc., Kensington, Maryland 20895.) Journal of cellular physiology, (1991 May) Vol. 147, No. 2, pp. 326-32. Journal code: 0050222. ISSN: 0021-9541. Pub. country: United States. Language: English.

AB The **envelope** glycoprotein (gp120) of **HIV**-1 was labeled with fluorescein by using 6-[4,6-dichlorotriazinyl]aminofluorescein. The labeled glycoprotein was found to bind to CD4-positive CEM cells. Monoclonal antibody OKT4a but not OKT4 blocked this binding. Similar specific binding of fluorescein-labeled gp120 with CD4 was observed in a solid-phase ELISA where sCD4 was attached to a polystyrene plate. The syncytium formation induced by **HIV**-1-infected cells on CEM cells was significantly inhibited in the presence of fluorescein-labeled gp120. Fluorescence photobleaching recovery measurements showed that the diffusion coefficient (D) of CD4 molecules complexed with fluorescein-labeled gp120 was approximately 5 x 10(-10) cm^2sec-1, with nearly 61% of the receptor molecules being mobile. Binding of anti-gp120 monoclonal antibody to the CD4-gp120 complex reduced the mobile fraction significantly. Diffusion of CD4 labeled with OKT4 IgG was markedly inhibited with reductions in both D and the mobile fraction, but such inhibition was not observed with OKT4 Fab. It appears that crosslinking of multiple molecules of CD4 by OKT4 antibody is required to reduce CD4 mobility. This suggests that the receptor might be present on the membrane plane as molecular clusters containing at least two molecules of CD4.

L8 ANSWER 10 OF 20 MEDLINE on STN

90281606. PubMed ID: 2353462. Differential viral gene expression and its effect on the biological properties of the cell clones of an **HIV**-1-infected cell line. Kalyanaraman V S; Rodriguez V; Josephs S; Gallo R C; **Sarngadharan M G**. (Department of Cell Biology, Advanced BioScience Laboratories, Kensington, Maryland 20895.) Virology, (1990 Jul) Vol. 177, No. 1, pp. 380-3. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB We have shown that 6D5 cells infected with the **HIV**-1 strain HTLV-III451 (6D5(451)) secreted viral **envelope** proteins **gp160** and gp120 into the culture medium. Single cell cloning of 6D5(451) cells separated three distinct phenotypes. All clones secreted unprocessed **env** protein **gp160** along with gp120. Only one phenotype produced infectious virus and contained normally processed gag proteins. The second phenotype was associated with nonproducer cells expressing only the **env** gene but no extracellular particles. The third phenotype synthesized Pr53gag but no reverse transcriptase, nor did it process the gag precursor. Only immature particles could be seen in the culture. Cells of the first and the third phenotypes produced two sizes of **gp160**, the normal and one with a small truncation at the C-terminus. Phenotype 2 only produced the smaller **gp160**. In all cases the **gp160** that was secreted into the medium was the truncated molecule.

L8 ANSWER 11 OF 20 MEDLINE on STN

90253924. PubMed ID: 2187500. Characterization of the secreted, native gp120 and **gp160** of the **human immunodeficiency virus** type 1. Kalyanaraman V S; Rodriguez V; Veronese F; Rahman R; Lusso P; DeVico A L; Copeland T; Oroszlan S; Gallo R C; **Sarngadharan M G**. (Bionetics Research Inc., Kensington, MD 20895.) AIDS research and human retroviruses, (1990 Mar) Vol. 6, No. 3, pp. 371-80. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB We have previously shown that the cell line 6D5(451) chronically infected with the **HIV**-1 isolate HTLV-III(451), secretes the **HIV**-1 **envelope** glycoproteins gp120 and **gp160** in the extracellular medium. The HTLV-III(451) gp120 and **gp160** were purified by sequential affinity

chromatographic steps using a monoclonal antibody to **HIV**-1 gp41 and an anti-**HIV**-1-positive human serum. Amino acid sequence analysis of gp120 and **gp160** showed the loss of the signal peptide. Digestion of the purified gp120 and **gp160** with endoglycosidases revealed that both proteins are heavily glycosylated and contain complex carbohydrates, in contrast to the intracellular form of **gp160** which has been shown to contain mannose-rich immature sugars. Competitive binding analysis showed that while both gp120 and **gp160** bind CD4, the affinity of **gp160** was five times lower than that of gp120. Both gp120 and **gp160** inhibited syncytia formation by **HIV**-1-infected cells when mixed with CD4+ cells. Furthermore, both gp120 and **gp160** had strong mitogenic effects on the T cells from **HIV**-1-infected gibbons but not on cells from uninfected gibbons.

L8 ANSWER 12 OF 20 MEDLINE on STN

90074394. PubMed ID: 2480151. Monoclonal antibodies to HTLV-III451 gp41: delineation of an immunoreactive conserved epitope in the transmembrane region of divergent isolates of **HIV**-1. Veronese F D; Rahman R; Kalyanaraman V S; Pal R; Lusso P; Tritch R; Petteway S; Gallo R C; **Sarngadharan M G**. (Department of Cell Biology, Bionetics Research, Inc., Kensington, MD 20895.) AIDS research and human retroviruses, (1989 Oct) Vol. 5, No. 5, pp. 479-86. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB We report on the development of monoclonal antibodies directed against the transmembrane portion of the **envelope** of HTLV-III451 gp41. One of these monoclonal antibodies, designated M71/2B4, was found to cross-react with transmembrane proteins from other independent isolates of **HIV**-1, namely IIIB, MN, and RF. Thus, this monoclonal antibody identifies an epitope located in a region of gp41 that is conserved among all these isolates. To identify this conserved region a series of E. coli recombinant proteins were screened in immunoblot with M71/2B4. From these results the epitope recognized by this antibody appears to map at the amino terminus of gp41, in the region indicated between the cleavage site with gp120 (aa 508) and the HindIII site (aa647).

L8 ANSWER 13 OF 20 MEDLINE on STN

89254401. PubMed ID: 2542177. Processing and secretion of **envelope** glycoproteins of **human immunodeficiency virus** type 1 in the presence of trimming glucosidase inhibitor deoxynojirimycin. Pal R; Kalyanaraman V S; Hoke G M; **Sarngadharan M G**. (Department of Cell Biology, Bionetics Research Inc., Rockville, Md 20850.) Intervirology, (1989) Vol. 30, No. 1, pp. 27-35. Journal code: 0364265. ISSN: 0300-5526. Pub. country: Switzerland. Language: English.

AB The processing and secretion of the **envelope** glycoprotein of **human immunodeficiency virus** type 1 (**HIV**-1) were studied in chronically infected cells treated with the trimming glucosidase inhibitor deoxynojirimycin (DNM). In Molt3 cells infected with human T-lymphotropic virus type III (HTLV-IIIB), DNM inhibited the intracellular proteolytic processing of **gp160** to gp120 and gp41. A clone of the HUT78 cell line called 6D5, when chronically infected with the **HIV**-1 isolate HTLV-III451 was shown to release both **gp160** and gp120 into the culture medium. The secretion of **envelope** glycoproteins from these infected cells was not inhibited by DNM treatment. The secreted proteins had higher molecular weights than **gp160** and gp120 from cultures not treated with DNM, presumably due to the presence of unprocessed carbohydrate residues on the polypeptide chain. These secreted glycoproteins from DNM-treated cells exhibited specific interaction with the CD4 molecule on the surface of target cells. However, the syncytium formation induced by **HIV**-1-infected cells on CD4+ cells was significantly inhibited in the presence of the glucosidase inhibitor. The minimal cytotoxicity of the DNM coupled with its strong inhibitory effect on the cell-to-cell spread of the virus suggest that it may be potentially useful in antiviral drug therapy of **HIV**-1 infection.

L8 ANSWER 14 OF 20 MEDLINE on STN

89240738. PubMed ID: 2541446. Role of oligosaccharides in the processing and maturation of **envelope** glycoproteins of **human immunodeficiency virus** type 1. Pal R; Hoke G M; **Sarngadharan M G**. (Department of Cell Biology, Bionetics Research, Inc., Kensington, MD 20895.) Proceedings of the National Academy of Sciences of the United States of America, (1989 May) Vol. 86, No. 9, pp. 3384-8. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The processing and maturation of **envelope** glycoproteins of **human immunodeficiency virus** type 1 (**HIV**-1) were studied in infected cells treated with inhibitors of oligosaccharide processing. In MOLT-3 cells chronically infected with **HIV**-1 (strain HTLV-IIIB), tunicamycin severely inhibited the glycosylation of **envelope** proteins. Deoxynojirimycin, an inhibitor of glucosidase I in the rough endoplasmic reticulum, inhibited the proteolytic processing of **gp160**, whereas no such effect was noted

with either deoxymannojirimycin or swainsonine, inhibitors of mannosidase I and II, respectively, in the Golgi complex. The processed gp120 and gp41 synthesized in the presence of deoxymannojirimycin were found to contain mannose-rich oligosaccharide cores as evidenced by their susceptibility to endoglycosidase H digestion. The formation of syncytia normally observed when CEM cells are cocultured with **HIV**-1-infected cells was markedly inhibited in the presence of deoxynojirimycin, but such inhibition was not observed in cells treated with deoxymannojirimycin or swainsonine. The infectivity of virions released from MOLT-3/HTLV-IIIB cells treated with deoxynojirimycin or deoxymannojirimycin was significantly lower than the infectivity of virions released from untreated cells. On the other hand, treatment with swainsonine did not affect the infectivity of the progeny virus. These results suggest that the proteolytic processing of **gp160** takes place in infected cells when the glycoprotein has mannose-rich oligosaccharide structures. Trimming of glucose residues and the primary trimming of mannose residues are necessary for the release of infectious virus.

L8 ANSWER 15 OF 20 MEDLINE on STN

89125740. PubMed ID: 2464704. Identification of simian immunodeficiency virus SIVMAC **env** gene products. Veronese F D; Joseph B; Copeland T D; Oroszlan S; Gallo R C; **Sarngadharan M G**. (Bionetics Research, Inc., Rockville, Maryland 20850-4373.) Journal of virology, (1989 Mar) Vol. 63, No. 3, pp. 1416-9. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB A monoclonal antibody recognizing an antigenic determinant on the **env** transmembrane protein, gp32 of simian immunodeficiency virus SIVMAC has been developed and designated SF8/5E11. The reactivity of this antibody was found to be type specific, since it did not cross-react with either SIVSMM or SIVMNe transmembrane proteins. The availability of both this antibody and the complete nucleotide sequence of SIVMAC allowed us to define the organization of the **env** gene products of this virus. Radiolabel sequencing of the amino termini of both **gp160** and gp32 confirmed the positions of both cleavage sites predicted by alignment of the inferred amino acid sequences of the SIVMAC and **human immunodeficiency virus** type 1 **env** genes. The cleavage site between the signal peptide and the external **env** glycoprotein resides between the cysteine residue at position 21 and the threonine residue at position 22, starting from the first residue after the **env** gene initiator methionine. The **env** precursor polyprotein **gp160** is cleaved between arginine 526 and glycine 527 to give rise to the external glycoprotein and the transmembrane of SIVMAC.

L8 ANSWER 16 OF 20 MEDLINE on STN

89062028. PubMed ID: 3264172. A unique **human immunodeficiency virus** culture secreting soluble **gp160**. Kalyanaraman V S; Pal R; Gallo R C; **Sarngadharan M G**. (Department of Cell Biology, Bionetics Research, Inc. Rockville, MD 20850.) AIDS research and human retroviruses, (1988 Oct) Vol. 4, No. 5, pp. 319-29. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB A clone of the HUT78 cell line, chronically infected with the **HIV**-1 isolate HTLV-III451, has been demonstrated to secrete unprocessed **HIV**-1 **envelope** precursor protein **gp160** as well as mature gp120. Further, when grown in serum-free defined medium these cells released approximately five times the amount of virus compared with cultures in normal medium. These proteins corresponded in their immunologic reactivities with the respective **envelope** proteins of the HTLV-IIIB isolate. They formed high-affinity soluble complexes with the CD4 antigen and inhibited the syncytium formation induced by HTLV-IIIB on CD4-positive cells. This is the first description of an **HIV**-1 culture system capable of shedding into the medium native **gp160** that is soluble in the absence of detergents.

L8 ANSWER 17 OF 20 MEDLINE on STN

89057920. PubMed ID: 3194424. Processing of the structural proteins of **human immunodeficiency virus** type 1 in the presence of monensin and cerulenin. Pal R; Gallo R C; **Sarngadharan M G**. (Department of Cell Biology, Bionetics Research, Inc., Rockville, MD 20850.) Proceedings of the National Academy of Sciences of the United States of America, (1988 Dec) Vol. 85, No. 23, pp. 9283-6. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The synthesis and processing of structural proteins of **human immunodeficiency virus** type 1 (**HIV**-1) were studied in infected cells treated with monensin and cerulenin. In MOLT-3 cells chronically infected with HTLV-IIIB, monensin inhibited the proteolytic cleavage of the **env**-coded polyprotein **gp160** to gp120, leading to the accumulation of the precursor **gp160**. The formation of syncytia normally observed when CEM cells are cocultivated with **HIV**-1-infected MOLT-3 cells was significantly inhibited in the presence of monensin. The effect of the ionophore on the culture was reversible, as withdrawal of monensin from

the medium restored the ability of the cells to form syncytia with CEM cells and led to the resumption of the processing of **gp160** to gp120. Monensin did not affect the synthesis and processing of gag-coded proteins and regulatory proteins. Cerulenin, an inhibitor of de novo fatty acid biosynthesis, inhibited the myristoylation and the proteolytic cleavage of the gag-coded polyprotein Pr53gag to p24 but did not affect the processing of **gp160**. However, use for monensin and cerulenin as antiviral agents for treatment of **HIV**-1 infection cannot be foreseen because of the pronounced in vitro toxicity observed.

L8 ANSWER 18 OF 20 MEDLINE on STN

87276425. PubMed ID: 3497054. Sequential changes in antibody levels to the **env** and gag antigens in **human immunodeficiency virus** infected subjects. Manca N; di Marzo Veronese F; Ho D D; Gallo R C; **Sarngadharan M G**. European journal of epidemiology, (1987 Jun) Vol. 3, No. 2, pp. 96-102. Journal code: 8508062. ISSN: 0393-2990. Pub. country: Italy. Language: English.

AB Sera from 51 HTLV-III (**human immunodeficiency virus, HIV**)-antibody positive subjects consisting of 21 asymptomatic individuals and 15 ARC and 15 AIDS patients were analyzed for their serological profiles toward the viral antigens. One of the asymptomatic subjects only showed a p24 reactivity in the immunoblot, but antibodies to the **env** antigens were clearly identified by immunoprecipitation of viral antigens (RIP) followed by SDS-polyacrylamide gel electrophoresis. RIP patterns of different subjects and even different bleeds from the same subjects showed a varying reactivity to the gag antigens whereas the reactivity towards the **env** antigens appeared to be generally stable. RIP analysis of sequential sera of virus-infected individuals indicated a pattern consistent with an initial steady rise of antibody reactivities to the gag antigens relative to the reactivities to the **envelope** antigens. These reactivities reached a plateau and then slowly declined. While all sera tested had antibodies to the **envelope** antigens **gp160**, gp120 and gp41, 86% of the asymptomatic subjects, 67% of the ARC patients and only 33% of the AIDS patients had antibodies to the gag proteins p24 and pr53gag.

L8 ANSWER 19 OF 20 MEDLINE on STN

87206235. PubMed ID: 2883731. HTLV-I--associated B-cell CLL: indirect role for retrovirus in leukemogenesis. Mann D L; DeSantis P; Mark G; Pfeifer A; Newman M; Gibbs N; Popovic M; **Sarngadharan M G**; Gallo R C; Clark J; +. Science, (1987 May 29) Vol. 236, No. 4805, pp. 1103-6. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB Serum containing antibodies to the human T-lymphotropic virus type I (HTLV-I) has been observed at a higher than expected frequency in patients with B-cell chronic lymphocytic leukemia (CLL) in an area endemic for HTLV-I. An attempt was made to determine whether the cells from patients with this leukemia were HTLV-I antigen-committed B cells that had undergone malignant transformation. Cells from two HTLV-I seropositive Jamaican patients with CLL were fused with a human B-lymphoblastoid cell line. The hybridoma cells that resulted from the fusion of CLL cells from patient I.C. produced an immunoglobulin (IgM) that reacted with the p24 gag protein from HTLV-I, HTLV-II, and HTLV-III (now referred to as **HIV**), but showed preferential reactivity with HTLV-I. The specific immunoglobulin gene rearrangement (IgM, kappa) in the CLL cell was demonstrated in the hybridoma cell line, indicating that the captured immunoglobulin was from the CLL cells. The IgM secreted by the fusion of CLL cells from patient L.L. reacted only with HTLV-I-infected cells and with the HTLV-I large **envelope** protein (gp61) on Western blots. The CLL cells from these patients appear to be a malignant transformation of an antigen-committed B cell responding to HTLV-I infection, suggesting an indirect role for this retrovirus in leukemogenesis.

L8 ANSWER 20 OF 20 MEDLINE on STN

87198956. PubMed ID: 2437327. **Human immunodeficiency virus** neutralizing antibodies recognize several conserved domains on the **envelope** glycoproteins. Ho D D; **Sarngadharan M G**; Hirsch M S; Schooley R T; Rota T R; Kennedy R C; Chanh T C; Sato V L. Journal of virology, (1987 Jun) Vol. 61, No. 6, pp. 2024-8. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Serum neutralizing antibodies against the **human immunodeficiency virus** were frequently detected in infected individuals, and low or absent serum neutralizing titers correlated with poor prognosis. Multiple diverse **human immunodeficiency virus** isolates were found to exhibit similar susceptibility to neutralization by a panel of human seropositive sera, suggesting that neutralizing antibodies are largely directed against conserved viral domains. Furthermore, utilizing antisera raised against a library of synthetic **env** peptides, four regions which are important in the neutralization process have been identified within both **human immunodeficiency virus envelope** glycoproteins (gp41 and gp120). Three of these are in conserved domains and should be considered for

inclusion in a candidate vaccine.

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E3            0 --> AMSELEM A S/AU
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E5            8     AMSELEM J/AU
E6            2     AMSELEM JOELLE/AU
E7           93     AMSELEM S/AU
E8           22     AMSELEM SERGE/AU
E9           49     AMSELGRUBER W/AU
E10          18     AMSELGRUBER W M/AU
E11           1     AMSELGRUBER W M WERNER M/AU
E12           3     AMSELGRUBER WERNER/AU

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L9   ANSWER 1 OF 28     MEDLINE on STN
TI   [On the activity of mucopolysaccharidases administered rectally].
     Sur l'activite des mucopolysaccharidases administrees par voie rectale.

L9   ANSWER 2 OF 28     MEDLINE on STN
TI   [Contribution to the study of the identification of synthetic dyes in
     pharmaceutical preparations].
     Contribution a l'etude de l'identification des colorants de synthese dans
     les preparations pharmaceutiques.

L9   ANSWER 3 OF 28     MEDLINE on STN
TI   [Application of turbidimetry to the assay of chondrosulfatase].
     Application de la turbidimetrie au dosage de la chondrosulfatase.

L9   ANSWER 4 OF 28     MEDLINE on STN
TI   [MEDICINE IN THE USSR. SOME CURRENT PROBLEMS].
     A M'EDECINE EN U.R.S.S. QUELQUES PROBL'EMES A L'ORDRE DU JOUR.

L9   ANSWER 5 OF 28     MEDLINE on STN
TI   [SKIN ABSORPTION].
     L'ABSORPTION CUTAN'EE.

L9   ANSWER 6 OF 28     MEDLINE on STN
TI   [METHOD FOR INDIRECT DETERMINATION OF VITAMIN B 12 IN VARIOUS
     PHARMACEUTICAL PREPARATIONS].
     M'ETHODE DE DOSAGE INDIRECT DE LA VITAMINE B 12 DANS DIVERSES
     PR'EPARATIONS PHARMACEUTIQUES.

L9   ANSWER 7 OF 28     MEDLINE on STN
TI   [SIMPLIFIED PHARMACOLOGICAL METHOD OF STUDY OF INDUCED INFLAMMATORY EDEMA:
     ITS APPLICATION TO A MUCOPOLYSACCHARIDASE-ALPHA-CHYMOTRYPSIN COMBINATION].
     METHODE PHARMACOLOGIQUE SIMPLIFIEE DE L'ETUDE DE L'OEDEME INFLAMMATOIRE
     PROVOQUE: SON APPLICATION 'A UNE ASSOCIATION DE MUCOPOLYSACCHARIDASES -
     ALPHACHYMOTRYPSINE.

L9   ANSWER 8 OF 28     MEDLINE on STN
TI   [DIFFUSION CAPACITY OF RABBIT SERUM AFTER REACTAL ADMINISTRATION OF
     MUCOPOLYSACCHARIDASES].
     POUVOIR DE DIFFUSION DU SERUM DE LAPIN APRES ADMINISTRATION RECTALE DE
     MUCOPOLYSACCHARIDASES.

L9   ANSWER 9 OF 28     MEDLINE on STN
TI   [RECENT METHODS OF FRACTIONATION OF ALPHA- AND BETA-LIPOPROTEINS].
     M'ETHODES R'ECENTES DE FRACTIONNEMENT DES ALPHA- ET BETA-LIPOPROT'EINES.

L9   ANSWER 10 OF 28     MEDLINE on STN
TI   Lipid metabolism disorders and laboratory examinations.

L9   ANSWER 11 OF 28     MEDLINE on STN
TI   Study of the distribution of the free and esterified fractions of
     cholesterol between the alpha and beta lipoproteins.

L9   ANSWER 12 OF 28     MEDLINE on STN
TI   Study of the relations between cholesterol and lipoproteins in
     arteriosclerosis.

L9   ANSWER 13 OF 28     MEDLINE on STN
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TI On a new technic for studying experimental blood lipid disorders.

L9 ANSWER 14 OF 28 MEDLINE on STN
TI Gaint lithiasis in a mega-ureter.

L9 ANSWER 15 OF 28 MEDLINE on STN
TI [Experimental contribution to the study of a new regulator of lipid metabolism].
Contribution experimentale a l'etude d'un nouveau regulateur du metabolisme lipidique.

L9 ANSWER 16 OF 28 MEDLINE on STN
TI [Ureterocele and habitual abortion].
Uretrocele et avortement habituel.

L9 ANSWER 17 OF 28 MEDLINE on STN
TI [A case of cancer of the urethra].
Sur un cas de cancer de l'urethre.

L9 ANSWER 18 OF 28 MEDLINE on STN
TI [A case of cancer of the urethra].
Sobre un caso de cancer de uretra.

L9 ANSWER 19 OF 28 MEDLINE on STN
TI [A case with indications for cystotomy in a woman].
Un cas d'indication de cystostomie chez la femme.

L9 ANSWER 20 OF 28 MEDLINE on STN
TI [Extravasation in urethrocystography].
L'extravasation dans l'urethrocystographie.

L9 ANSWER 21 OF 28 MEDLINE on STN
TI [Renal cysto-adenoma].
Cystoadenome renal.

L9 ANSWER 22 OF 28 MEDLINE on STN
TI [Sarcoma of the prostate].
Sarcome de la prostate.

L9 ANSWER 23 OF 28 MEDLINE on STN
TI [Renal adenoma].
Adenome renal.

L9 ANSWER 24 OF 28 MEDLINE on STN
TI [Renal cystadenoma].
Cistoadenoma renal.

L9 ANSWER 25 OF 28 MEDLINE on STN
TI [Vascular accidents in urethrocystography].
Accidentes vasculares de la uretrocistografaa.

L9 ANSWER 26 OF 28 MEDLINE on STN
TI [Meningeal metastasis of a carcinoma of the prostate; its possible production mechanism].
Metastasis meningea de un carcinoma de prostata; su posible mecanismo de produccion.

L9 ANSWER 27 OF 28 MEDLINE on STN
TI [Gigantic bilateral hydronephrosis without apparent organic obstacle (renal pseudosclerosis)].
Hidronefrosis bilateral gigante sin obstaculo organico aparente (pseudosclerosis renal).

L9 ANSWER 28 OF 28 MEDLINE on STN
TI Pseudo-sclerose renale bilaterale.

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FULL ESTIMATED COST	34.00	34.21

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Feb 2007 (20070215/PD)
FILE LAST UPDATED: 15 Feb 2007 (20070215/ED)
HIGHEST GRANTED PATENT NUMBER: US7178169
HIGHEST APPLICATION PUBLICATION NUMBER: US2007039082

CA INDEXING IS CURRENT THROUGH 15 Feb 2007 (20070215/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Feb 2007 (20070215/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006

=> s emulsome?/clm
L10 2 EMULSOME?/CLM

=> d l10,cbib,1-2

L10 ANSWER 1 OF 2 USPATFULL on STN
2006:282133 Modified oligoribonucleotide analogs with enhanced immunostimulatory activity.
Uhlmann, Eugen, Glashuetten, GERMANY, FEDERAL REPUBLIC OF
Krieg, Arthur M., Wellesley, MA, UNITED STATES
Lipford, Grayson B., Watertown, MA, UNITED STATES
Coley Pharmaceutical GmbH, Langenfeld, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)Coley Pharmaceutical Group, Inc., Wellesley, MA, UNITED STATES (non-U.S. corporation)
US 2006241076 A1 20061026
APPLICATION: US 2006-411975 A1 20060426 (11)
PRIORITY: US 2005-674896P 20050426 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 2 OF 2 USPATFULL on STN
2001:212420 Immunostimulatory nucleic acids for inducing a Th2 immune response.
McCluskie, Michael J., Ottawa, Canada
Davis, Heather L., Ottawa, Canada
US 2001044416 A1 20011122
APPLICATION: US 2001-768012 A1 20010122 (9)
PRIORITY: US 2000-177461P 20000120 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s emulsome?
L11 64 EMULSOME?

=> s l11 and vaccin?
54222 VACCIN?
L12 60 L11 AND VACCIN?

=> s l12 and ay<1997
2437461 AY<1997
L13 2 L12 AND AY<1997

=> d l13,cbib,1-2

L13 ANSWER 1 OF 2 USPATFULL on STN
2003:85841 **VACCINE** AGAINST GRAM NEGATIVE BACTERIA.
ZOLLINGER, WENDELL D., SILVER SPRING, MD, UNITED STATES
SHOEMAKER, DAVID R., SILVER SPRING, MD, UNITED STATES
SAUNDERS, AGNES G., SILVER SPRING, MD, UNITED STATES
BRANDT, BRENDA L., GAITHERSBURG, MD, UNITED STATES
US 2003059444 A1 20030327
APPLICATION: US 1996-749592 A1 19961115 (8)
PRIORITY: US 1996-28542P 19961015 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 2 OF 2 USPATFULL on STN
1998:14497 Solid fat nanoemulsions as **vaccine** delivery vehicles.
Anselem, Shimon, Rehovot, Israel
Lowell, George H., Baltimore, MD, United States
Aviv, Haim, Rehovot, Israel
Friedman, Doron, Carmei Yosef, Israel
Pharmos Corporation, New York, NY, United States (U.S. corporation)The United States of America as represented by the Secretary of the Army, Washington, DC, United States (U.S. government)
US 5716637 19980210
WO 9426255 19941124
APPLICATION: US 1995-553350 19951116 (8)
WO 1994-US5589 19940518 19951116 PCT 371 date 19951116 PCT 102(e) date
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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